REGARDING ANTIDEPRESSANTS AND EFFICACY IN SHORT-TERM CLINICAL TRIALS

DEAR EDITOR:

I would like to add two more factors besides the ones Dr. Feifel discusses in his article, "More depressing news on antidepressants: Should we panic?" which appeared in the April issue of *Psychiatry 2008*.[1]

One: There is a strong incentive for the clinical investigators to push marginally depressed patients into drug trials. Since the reimbursement is based upon number of patients enrolled, there is an unconscious bias to rate the depressive symptoms higher than they are to help patients meet the inclusion criteria.

The patients with milder and atypical forms of depression often show high therapeutic response to placebo and psychosocial interventions thus diluting the evidence of an antidepressant's efficacy with the more severely depressed. Furthermore, the mildly depressed are more likely to show decline of their symptoms spontaneously irrespective of the treatment. This also works against showing differences between the antidepressant and the placebo.

Two: Once the patient is enrolled in the study, there is a strong incentive to rate the treatment response liberally. The investigator has a powerful motivation to see that the drug works. If the drug is effective, it means publication and the honor of bringing a new drug to the market. Thus, when rating the treatment response, there is an unconscious bias to show greater improvement than what is actually occurring. This once again dilutes the differences between the antidepressant and placebo response.

The above two factors were borne upon me while doing my first clinical trial—a four-week, double-blind, placebo–controlled study in depression. I observed how eager we were to enroll anyone who declared himself or herself to be depressed during the screening rounds that we conducted with all the new admissions throughout the state hospital where the research unit was situated. To enable patients to meet the study's inclusion criteria, there was a strong inner compulsion to downplay comorbid conditions and to exaggerate the intensity of the depression. It did not take me long to realize that all the research subjects were improving quite rapidly, and, therefore, the study would run into the problem of falsely showing that the antidepressant was no better than placebo.

REFERENCES

1. Feifel D. More depressing news on antidepressants: Should we panic? *Psychiatry* (Edgemont) 2008;5(4)–35–36.

With regards,
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